TGFβ-3 ~~and FGF~~ (a) with at least one fibrotic growth factor present in the composition in a lower proportion to such non-fibrotic growth factor than occurs naturally in the wounds or disorders, or (b) with at least one fibrotic growth factor together with at least one anti-fibrotic agent against the fibrotic growth factor, in a pharmaceutically acceptable carrier.

REMARKS

Claims 1-21 are now pending in the application. These claims are the original claims as filed and amended in the Preliminary Amendment filed September 15, 1994. Claims 1, 5-7 and 20 have been amended. Claim 21 has been added. The amendments to the claims and the new claim are believed to be wholly supported within the specification and claims as originally filed. Claim 1 has been amended to include fragments of the non-fibrotic growth factor. The addition is supported in the third paragraph of page 15. Support for new claim 21 is found in originally filed claims 2 and 3 and at page 15, third paragraph.

Applicants' Invention

Applicants' invention relates to the use of non-fibrotic growth factors and fragments to promote healing with little or no scarring as compared to natural healing processes. Applicants' composition includes a non-fibrotic growth factor or fragment which is used in combination with either (1) no fibrotic growth factor, (2) fibrotic growth factors present in the composition in a lower proportion to such non-fibrotic growth factor that occurs naturally in wounds or disorders in question, or (3) with such fibrotic growth factors together with anti-fibrotic agents against them. These agents are incorporated into a pharmaceutically

acceptable carrier. Applicants have discovered a means to promote healing by using non-fibrotic growth factors or fragments to overcome scarring which would normally occur. Certain claims are directed to specific growth factors, such as TGFβ-3 and FGF.

Rejections under 35 U.S.C. §102(b)

Applicants acknowledge that claims 8-11 and 13 do not have any rejections based on prior art.

Claims 1, 3, 6, 17 and 18 stand rejected under 35 U.S.C. §102(b) as being anticipated by the PCT publication WO 90/03810 (hereafter Geistlick et al). The rejection states that Geistlick et al teach delayed release compositions for wound healing. The compositions are then dispersed in a hydrogel. The rejection states that mere recitation of newly discovered functional properties, inherently possessed by the thing, does not cause a claim to distinguish over the prior art.

Geistlick et al relates to delayed release agents for wound healing. The wound healing agents are placed into a hydrogel containing one or more gellable proteins, peptides or polysacharides dispersed with a hydrophilic polymer. The growth factors are selected from epidermal growth factor, human fibroplast growth factor, human insulin-growth factor and platelet growth factor. Geistlick et al's only example relates to epidermal growth factor. Geistlick et al does not teach or suggest the use of the specific combinations of agents required by Applicants' claims. No teaching in Geistlick et al relates to non-fibrotic growth factors used alone or used in combination with fibrotic growth factors, and fibrotic growth factors together with anti-fibrotic agents. Since Geistlick et al does not teach each element of

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Applicants' claims, Applicants submit that Geistlick et al does not anticipate their claims. Accordingly, Applicants request withdrawal of the rejection.

Claims 1, 2, 6, 7, 12 and 14-20 stand rejected under 35 U.S.C. §102(b) as anticipated by Cerlitti et al. The rejection states that Cerlitti et al teach a method for treating wounds with TGF β like proteins. The rejection notes that Cerlitti et al teaches TGFβ-1, TGFβ-2 and TGFβ-3. The rejection states it would be inherent to possess the properties of Applicants' claims.

Cerlitti et al relates to a process for producing biologically active, dimeric TGF-β compositions and pharmaceutical compositions comprising it. Cerlitti et al fails to recognize any differences between any of the TGF-β like proteins. Specifically, there is no teachings to the non-fibrotic character of TGFβ-3. Cerlitti et al fails to teach or suggest the use of the non-fibrotic agent alone or in specific proportions with fibrotic agents or anti-fibrotic agents as required by Applicants' claims. Without teachings of the specific claimed combinations, Cerlitti et al cannot anticipate Applicants' claims. Accordingly, Applicants request withdrawal of this rejection.

Claims 1, 4 and 5 stand rejected under 35 U.S.C. §102(b) as anticipated by Ruoslahti et al (WO 91/10727). The rejection states Ruoslahti et al teaches a method of treating a pathology caused by a TGF regulated activity including fibrotic disease. The rejection also states that Ruoslahti et al teaches anti-fibrotic agents. The rejection states that the compositions of Ruoslahti et al would inherently possess the properties of Applicants' claimed compositions.

Ruoslahti et al relates to a method of inhibiting cell regulatory factor activity using a purified polypeptide. More specifically, Ruoslahti et al teaches the ability of Decorin, to bind TGFβ. Ruoslahti et al teaches the general effect of TFGβ's family of regulatory factors but contains no teaching specifics to TGFβ-3 or its non-fibrotic characteristic. Ruoslahti et al does not teach or suggest the specific combinations of Applicants' claims, namely the combination of a non-fibrotic agent or fragment with either no growth factors, with growth factors present in an amount lower in proportion to non-fibrotic growth factors that occur naturally in a wound or disorder or a fibrotic growth factor or fragment together with anti-fibrotic growth factors. Without the teachings of such combinations, Applicants submit that Ruoslahti et al does not anticipate their claims.

All the references cited by the Examiner fail to teach or suggest the specific combinations of fibrotic growth factors or fragments with the other elements of Applicants' claims. Additionally, there is no recognition in any of the references of the non-fibrotic characteristics of FGF and TGFβ. Accordingly, withdrawal of the rejections based on these references is respectfully requested.

35 U.S.C. §112 Rejections

The specification is objected to and claims 4 and 5 are rejected under 35 U.S.C. §112, first paragraph, as failing to provide adequate written support. Specifically, the use of the term anti-fibrotic agents is questioned.

At page 15, second paragraph, Applicants define anti-fibrotic agents as being anti-scarring agents. Page 1, paragraph 2, defines fibrosis. Anti-fibrotic agents may be defined

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as agents which promote reduced fibrosis. An example of an anti-fibrotic agent is an agent which inhibits scarring during wound healing. Applicants note that anti-fibrotic agents are discussed in Roslahti et al. A person skilled in the art upon reviewing the specification as a whole would determine that the anti-fibrotic agents are agents which inhibit the activity of fibrotic agents. Accordingly, a person of skill in the art would be able to determine how to make and use Applicants' invention. Accordingly, Applicants request withdrawal of this rejection.

Claims 1-20 stand rejected under 35 U.S.C. §112 for various reasons. The claims are objected to for the use of the term "(s)" and "and/or". Applicants have amended their claims to eliminate these objections. Withdrawal of this rejection is requested. Use of the term "compositions" in the preamble of claim 1 is questioned. In view of Applicants' amendment, this rejection is considered moot. The term "for example" is questioned in the claims. Applicants have amended their claims to eliminate this objection.

Claims 8-11 and 13 are objected to under 37 C.F.R. 1.75 as being in improper form as depending from a multiple dependent claim, namely claim 5. Claim 5 as originally filed was not a multiple dependent claim. In the Preliminary Amendment submitted September 15, 1994 Applicants' requested examination to proceed on the 19 claims as originally filed. A copy of those original claims was included with the Preliminary Amendment. Applicants added one claim with their Preliminary Amendment. The transmittal sheet for the Office Action indicates that 20 claims are pending in the application. The amended claims in the PCT Annex have 20 claims, not 19 as originally filed. The number of claims pending reflects the original claims plus claim 20 from the Preliminary Amendment. Applicants

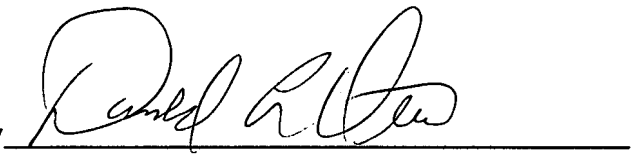
believe that the rejection is improper because claim 5 as originally filed is not in multiple dependent form. Applicants request withdrawal of this rejection. In the event questions regarding claim 5 persist, Applicants request that the Examiner call the undersigned to discuss any questions.

An Abstract has been added with this Amendment.

In view of the amendments to the claims and the above comments, Applicants submit that the claims are now in condition for allowance. In the event any issues remain in the prosecution of this application, Applicants request that the Examiner call the undersigned attorney to expedite allowance of the claims. If any fees are required for the filing of these papers, Applicants request the Commissioner to charge those fees to deposit account #18-0988.

Respectfully submitted,

RENNER, OTTO, BOISSELLE & SKLAR, P.L.L.

By 

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